

## **REMARKS**

### **I. Status of the application**

Claims 3 and 20 – 42 are pending in the application, with claims 3 and 36-38 withdrawn from consideration. Claims 20-35 and 39-42 stand rejected. Claim 20 has been amended and support for such amendment can be found throughout the specification, drawings, and claims as originally filed.

### **II. Claims 20, 22, 29 – 32, 35, 39 and 40 are patentable over Mazzeo in view of Luner et al and Witt**

Claims 20, 22, 29 – 32, 35, 39 and 40 stand rejected under 35 U.S.C. 103(a) over Mazzeo et al (capillary isoelectric focusing of proteins in uncoated fused-silica capillaries using polymeric additives, Anal. Chem. 1991, 63, 2852-2857) in view of Luner et al (U.S. Pat No. 3,664,939) and Witt et al U.S. Pat. No. 7,118,660. This rejection is respectfully traversed.

The references, alone or in combination, fail to disclose the invention defined by the subject claims, i.e., a method of determining the isoelectric point of charged analyte(s) by focusing the charged analyte in a flowing liquid in an electric field gradient, changing the pH of the flowing liquid at least once by an amount sufficient to shift the location of the band(s) of the charged analyte, obtaining pH and corresponding position data of the charged analyte, and determining the isoelectric point of the charged analyte based on the pH and corresponding position data.

Mazzeo fails to teach or suggest focusing a charged analyte in a flowing liquid in an electric field gradient and adjusting the pH of the flowing liquid to shift the charged analyte to a new focused location. Rather, Mazzeo utilizes capillary isoelectric focusing to focus a protein(s) in a pH gradient at a single location. The focused protein(s) is then transported past a detection window by electroendosmotic flow. In other words, some electroendosmotic flow is maintained for the mobilization of focused zone(s) of protein(s) past the UV detection window “during the focusing step.” (See Mazzeo at col. 1). Therefore, the proteins are focused in one location in the

electroendosmotic flow, and the flow proceeds to move the medium along with the focused protein past a detection window without the proteins ever focusing in a separate distinct location relative to the medium.

Luner and Witt fail to cure the deficiency of Mazzeo. Luner discloses a method for isoelectric focusing proteins into an isoelectric spectrum utilizing a pH gradient and an electric current. See Abstract of Luner. Witt discloses a method for isoelectric focusing proteins in various bands utilizing a pH gradient and a high voltage. See col. 5, lines 5-37 of Witt. Each reference fails to teach or suggest an isoelectric focusing method that focuses a protein in one focused location and then shifts that protein to a new focused location. Therefore, the references, alone or in combination, fail to disclose a method of determining the isoelectric point of a charged analyte comprising focusing a charged analyte in a flowing liquid in an electric field gradient and adjusting the pH of the flowing liquid to shift the charged analyte to a new focused location.

Further, as the Examiner has acknowledged, Mazzeo fails to disclose determining an isoelectric point for a charged analyte by utilizing pH and corresponding position data of the charged analyte, at a plurality of positions, in an electric field gradient. Luner and Witt fail to cure the deficiency of Mazzeo.

Luner merely discloses that the pH of the focused ampholyte may be used to determine the isoelectric point of the same ampholyte. See col. 1, lines 29-33 of Luner. Witt discloses that the initial focusing point of a protein in a pH gradient may be determined based on the speed by which the protein moves from the gradient past a detector. See col. 5, lines 33-37. Each reference fails to teach or suggest determining an isoelectric point for a charged analyte by utilizing pH and corresponding position data of the charged analyte, at a plurality of positions, in an electric field gradient.

Therefore, the references, alone or in combination, fail to disclose a method of determining the isoelectric point of a charged analyte comprising focusing a charged analyte in a flowing liquid in an electric field gradient, adjusting the pH of the flowing liquid to shift the charged analyte to a new focused location, obtaining pH and corresponding position data of the

charged analyte, and determining the isoelectric point of the charged analyte based on the collected data. Therefore, Applicants request that the rejection be reconsidered and withdrawn.

Additionally, to further clarify the claims on this point, claim 20 has been amended to call out more expressly that each charged analyte is focused in multiple distinct locations. Claim 20 now expressly recites a method of determining the isoelectric point of a charged analyte, comprising focusing a charged analyte in a flowing liquid in an electric field gradient to form in the flowing liquid a focused band of the charged analyte at a *first* stable position in the electric field gradient; changing the pH of the flowing liquid at least once by an amount sufficient to change the position of the focused band of the charged analyte within the electric field gradient to a *second* stable position in the electric field gradient; obtaining pH and corresponding position data for the charged analyte, comprising determining the pH of the flowing liquid and the corresponding position of the focused band of the charged analyte at a plurality of band positions within the electric field gradient; and determining the isoelectric point of the charged analyte based on the pH and corresponding position data.

**III. Claims 21, 24, 26 and 33 are patentable over Mazzeo, Luner, Witt et al, and further in view of Yang**

Claims 21, 24, 26 and 33 stand rejected under 35 U.S.C. 103(a) over Mazzeo, Luner, Witt and further in view of Yang et al (U.S. Pat. No. 4,666,855). This rejection is respectfully traversed.

As previously discussed Mazzeo, Luner, and Witt fail to disclose a method of determining the isoelectric point of charged analyte(s) by focusing the charged analyte in a flowing liquid in an electric field gradient, changing the pH of the flowing liquid at least once by an amount sufficient to shift the location of the band(s) of the charged analyte, obtaining pH and corresponding position data of the charged analyte, and determining the isoelectric point of the charged analyte based on the pH and corresponding position data. Yang fails to cure the deficiencies of Mazzeo, Luner, and Witt. Applicant requests that the rejection be reconsidered and withdrawn.

**IV. Claim 23 is patentable over Mazzeo, Luner, Witt and further in view of Malabarba**

Claim 23 stands rejected under 35 U.S.C. 103(a) over Mazzeo, Luner, Witt and further in view of Malabarba et al (U.S. Pat. No. 5,521,155). This rejection is respectfully traversed.

As previously discussed Mazzeo, Luner, and Witt fail to disclose a method of determining the isoelectric point of charged analyte(s) by focusing the charged analyte in a flowing liquid in an electric field gradient, changing the pH of the flowing liquid at least once by an amount sufficient to shift the location of the band(s) of the charged analyte, obtaining pH and corresponding position data of the charged analyte, and determining the isoelectric point of the charged analyte based on the pH and corresponding position data. Malabarba fails to cure the deficiencies of Mazzeo, Luner, and Witt. Applicant requests that the rejection be reconsidered and withdrawn.

**V. Claim 25 is patentable over Mazzeo, Luner, Witt and further in view of Zhu**

Claim 25 stands rejected under 35 U.S.C. 103(a) over Mazzeo, Luner, Witt and further in view of Zhu et al (U.S. Pat. No. 5,110,434). This rejection is respectfully traversed.

As previously discussed Mazzeo, Luner, and Witt fail to disclose a method of determining the isoelectric point of charged analyte(s) by focusing the charged analyte in a flowing liquid in an electric field gradient, changing the pH of the flowing liquid at least once by an amount sufficient to shift the location of the band(s) of the charged analyte, obtaining pH and corresponding position data of the charged analyte, and determining the isoelectric point of the charged analyte based on the pH and corresponding position data. Zhu fails to cure the deficiencies of Mazzeo, Luner, and Witt. Applicant requests that the rejection be reconsidered and withdrawn.

**VI. Claims 27 and 28 are patentable over Mazzeo, Luner, Witt and further in view of Ivory**

Claims 27 and 28 stand rejected under 35 U.S.C. 103(a) over Mazzeo, Luner, Witt and further in view of Ivory et al (U.S. Pat. No. 6,277,258). This rejection is respectfully traversed.

As previously discussed Mazzeo, Luner, and Witt fail to disclose a method of determining the isoelectric point of charged analyte(s) by focusing the charged analyte in a flowing liquid in an electric field gradient, changing the pH of the flowing liquid at least once by an amount sufficient to shift the location of the band(s) of the charged analyte, obtaining pH and corresponding position data of the charged analyte, and determining the isoelectric point of the charged analyte based on the pH and corresponding position data. Ivory fails to cure the deficiencies of Mazzeo, Luner, and Witt. Applicant requests that the rejection be reconsidered and withdrawn.

**VII. Claim 34 is patentable over Mazzeo, Luner, Witt and further in view of Ness**

Claim 34 stands rejected under 35 U.S.C. 103(a) over Mazzeo, Luner, Witt and further in view of Ness et al (U.S. Pat. No. 6,613,508). This rejection is respectfully traversed.

As previously discussed Mazzeo, Luner, and Witt fail to disclose a method of determining the isoelectric point of charged analyte(s) by focusing the charged analyte in a flowing liquid in an electric field gradient, changing the pH of the flowing liquid at least once by an amount sufficient to shift the location of the band(s) of the charged analyte, obtaining pH and corresponding position data of the charged analyte, and determining the isoelectric point of the charged analyte based on the pH and corresponding position data. Ness fails to cure the deficiencies of Mazzeo, Luner, and Witt. Applicant requests that the rejection be reconsidered and withdrawn.

**VIII. Claims 41 and 42 are patentable over Mazzeo, Luner, Witt and further in view of Ivory**

Claims 41 and 42 stand rejected under 35 U.S.C. 103(a) over Mazzeo, Luner, Witt and further in view of Ivory et al (U.S. Pat. No. 6,277,258). This rejection is respectfully traversed.

As previously discussed Mazzeo, Luner, and Witt fail to disclose a method of determining the isoelectric point of charged analyte(s) by focusing the charged analyte in a flowing liquid in an electric field gradient, changing the pH of the flowing liquid at least once by

an amount sufficient to shift the location of the band(s) of the charged analyte, obtaining pH and corresponding position data of the charged analyte, and determining the isoelectric point of the charged analyte based on the pH and corresponding position data. Ivory fails to cure the deficiencies of Mazzeo, Luner, and Witt. Applicant requests that the rejection be reconsidered and withdrawn.

#### **IX. Conclusion**

Applicant requests that the amendments as presented above be entered in the referenced patent application, and that the application be reconsidered. Applicant submits that all claims pending in the application are now in condition for allowance.

A petition for a three-month extension of time under 37 C.F.R. 1.136(a) and the accompanying fee are filed herewith. The Commissioner is hereby authorized to charge any such fees or credit any overpayment of fees to Deposit Account No. 19-0733.

Respectfully submitted,

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